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Evaluation of Fasciotomy and Vasodilator for Treatment of Frostbite in the Dog[1,2]

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The importance of frostbite as a military medical problem is well known. Over one million cases have been recorded during the two World Wars and the Korean War, excluding Soviet and Chinese casualties (1). However, since cases are scattered and escape compilation, it is not generally appreciated that frostbite is a significant civilian medical problem, particularly in the subarctic areas of the world. Several hundred cases of severe frostbite have been documented in Alaska alone in the past 20 years (2, 8).

Failure of the microcirculation and resultant hypoxia have been implicated as the key in the pathogenesis of most clinical frostbite (3, 6, 13). Vascular stasis and peripheral ischemia have been attributed to a series of phenomena including endothelial pathology (3) and platelet aggregation as well as other coagulopathies (11, 15). Increased tissue pressure, secondary to edema formation, may explain why traditional forms of chemotherapy alone have not been particularly effective (7). Mills (7) and Edwards (4) have suggested fasciotomy as a means of quickly and easily reducing the increased tissue pressure seen following rewarming of the frostbitten extremity. Fasciotomy has been used successfully to treat arterial/venous injury, massive soft tissue injury, and other syndromes involving alternation of the normal distal circulation and associated massive swelling (10). One of us has been encouraged by his initial clinical experience in humans using fasciotomy along with vasodilators to treat frostbite (8).

The objective of this study was to evaluate the effectiveness of fasciotomy and vasodilator therapy for frostbite in the dog model. Treatment techniques were evaluated based on the measurement of foot volume, deep tissue temperature, tissue pressure, and tissue survival.

MATERIALS AND METHODS

Severe frostbite was produced in the left rear foot of 26 mongrel dogs ranging from 15

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[2] In conducting the research described in this report, the investigators adhered to the "Guide for Laboratory Animal Facilities and Care" as promulgated by the committee on the Guide for Laboratory Animal Resources, National Academy of Sciences, National Research Council.

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to 20 kg body weight. The dogs were separated into groups by the treatment which each group received. Six dogs (group A) served as controls and received only the injury and daily therapy described below. Six dogs (group B) in addition to the basic therapy received 10 mg phenoxybenzamine HCl (Dibenzyline®, SKF) via gastric tube at the onset of rapid rewarming following the freezing injury and daily per os. Six dogs (group C) in addition to basic therapy received a fasciotomy at 30 min postthaw. Fasciotomy incisions extended (a) longitudinally on the medial and lateral aspects of the injured foot from just proximal to the hock to phalanx III, (b) on the plantar surface from 3 cm distal to the tuber calsis to the metatarsal pad, and (c) on the dorsal surface over digits III and IV from mid metatarsal to phalanx III. Eight dogs (group D) in addition to basic therapy received both phenoxybenzamine and fasciotomy.

Preliminary Procedures

Twenty-four hours prior to the production of the frostbite injury, chronic copper-constantan thermocouples were implanted bilaterally at the level of the metatarsal-phalangeal junction, and anterior–posterior and lateral radiographs taken. Thirty minutes prior to freezing, baseline data were recorded bilaterally: unanesthetized deep foot temperatures, foot volume by water displacement, foot length, and 35 mm photographs. Anesthesia was induced by intravenous administration of thiamylal (Surital®, Parke Davis) and maintained with pentobarbital (Nembutal®, Abbott Labs.). Dogs were placed in sternal recumbency, with rear legs suspended over the end of a modified table. To preclude pressure on femoral vessels, phalangeal IM pins were transversed through the tuber calci, suspending the legs from supporting members attached to the table. The left foot was covered with a rubber sleeve and a tourniquet placed on both feet just proximal to the hock; the right foot acted as a control for ischemia. The surgical tubing tourniquet was applied in a manner which stopped both venous and arterial blood flow in the foot (Fig. 1).

Freezing Injury

The left foot was immersed in a −27 to −28°C circulating ethylene glycol bath, to a level of 4.5 cm distal to the point of the hock (the tarsal-metatarsal junction). The tourniquets remained on both rear feet for 100 min while the left foot was being freeze injured. A central venous pressure catheter was positioned in the anterior vena cava, via the right jugular vein, during the freeze period. Immediately after removal from the ethylene glycol bath, both tourniquets were removed, the rubber sleeve was removed from the left foot, and the left foot was rapidly rewarmed in a still water bath at 42°C. Rewarming was considered complete when the deep temperature of the frozen extremity (left) equaled that of the contralateral (right) foot. Immediately after removal from the thawing bath, a postthaw photo was taken and foot volumes were measured by water displacement. Foot volumes and photos were recorded additionally at 30 min, 1 and 2 hr postthaw. Following rewarming, adequate lactated ringers solution (Travenol, Inc.) was administered to maintain the central venous pressure between −1 and +3 cm H_2O. Tissue pressure was measured by a water manometer at a point midway between the skin and metatarsals on the plantar surface of the foot (14). Tissue pressure was recorded at 25 to 30 min and 1 hr postthaw. Throughout the entire freeze–thaw period and for 3 hr postthaw, bilateral deep foot temperatures and rectal temperatures were recorded on a Leeds and Northrup Speedomax® recorder. At 2½ to 3 hr postthaw, dogs were removed from the holding apparatus, modified Robert Jones bandages were applied to

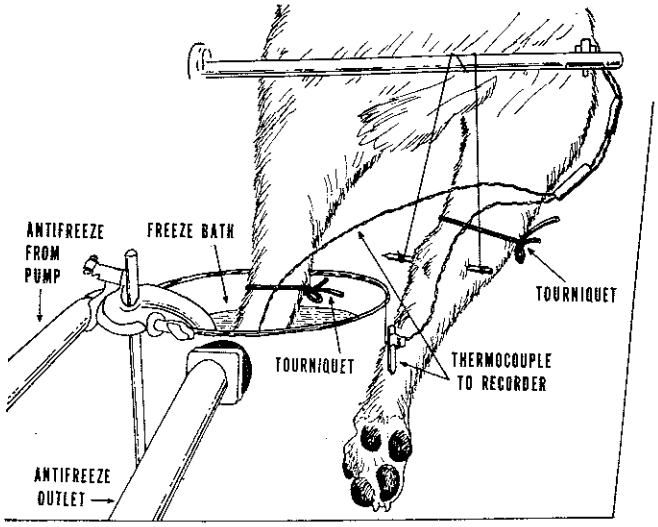

FIG. 1. Line drawing illustrating subject positioned in freezing apparatus.

both rear legs, and the dogs were returned to their cages to recover from anesthesia.

Daily Nursing Care

Daily nursing care included a 20 min treatment in a 38°C water bath containing Povidone-Iodine Soln (Betadine Soln®, Purdue Fredrick Co.). A "whirlpool" effect was produced by bubbling compressor air through a tube in the bottom of the bath. Before each daily "whirlpool" treatment, deep foot temperatures and foot volumes were measured, and a photographic and written description of the condition of the injured extremity recorded. On Days 1 to 3, all dogs received 300 ml lactated ringers solution i.v. during the "whirlpool" therapy. After treatment, Robert Jones bandages were once again applied to both rear legs. Systemic antibacterial therapy was not used in any of the dogs in this study.

All 26 dogs received the injury and therapy described above and were maintained for 14 days postthaw, at which time a second radiograph was taken and the dogs were euthanized. Tissue survival was graded on a single blind basis on a scale from 0 to 9, total tissue loss to total tissue survival, respectively, (Fig. 2) based

9. Very superficial or no tissue loss.
8. Loss of dorsal skin only.
7. Loss of portions of 1 to 2 toes and dorsal skin.
6. Loss of dorsal skin, muscle, and portions of toes.
5. Loss of dorsal muscle and portions of toes, with loss of structural integrity between plantar muscle and metatarsals.
4. Loss of dorsal surface and medial or lateral plantar surface, leaving one or two metatarsals (with muscle) and portions of one or two toes.
3. Tag of tissue, one metatarsal wide or less, or a portion of tissue greater than 3.5 cm in length but less than above.
2. Tag of 2.5 to 3.5 cm in length beyond tarsal-metatarsal junction.
1. Tag of 1.5 cm but less than 2.5 cm beyond tarsal-metatarsal junction.
0. Amputation at level of tarsal-metatarsal junction.

FIG. 2. Frostbite injury grading key used to assign tissue loss/salvage score from photographs taken at 14 days postinjury.

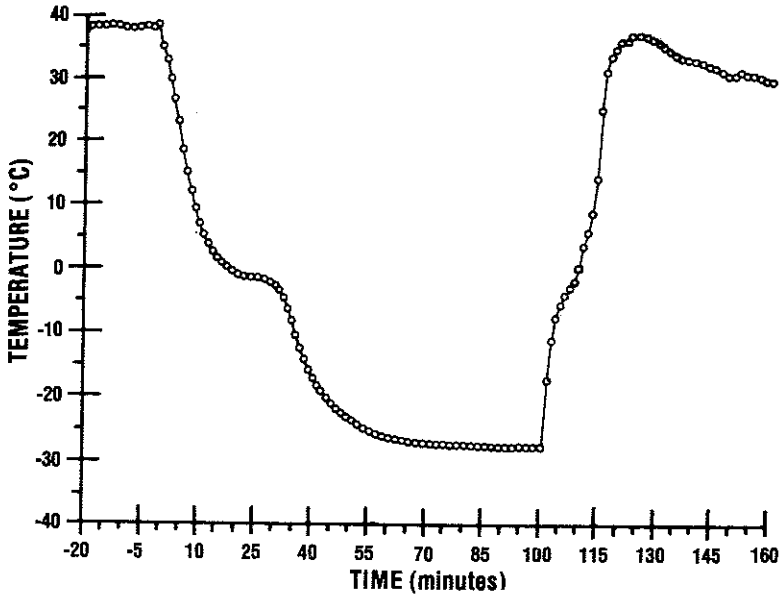

FIG. 3. Time-temperature curve illustrating typical deep foot temperature during freeze–thaw cycle.

on the photographs and radiographs taken 14 days after the freezing injury.

Statistics

Data for all dependent variables were analyzed by analysis of variance.

RESULTS

Figure 3 illustrates a typical freeze–thaw curve used to produce the standard injury in the 26 dogs. In attempting to define a suitable injury, we started with the time-temperature curve used by Sumner (12) to produce a tarsal-metatarsal amputation in the dog hind foot. We found that by using the 70 to 80 min Sumner freezing curve we could produce an injury only severe enough to cause the loss of portions of two to three toes. It was not until the foot was maintained in the freezing bath for 100 min that a consistent tarsal-metatarsal amputation could be produced. After application of the tourniquet and insertion into the ethylene glycol bath, the deep temperature of the foot dropped precipitously to 0°C (approx. 20 min.) Foot temperatures plateaued on or near −1°C (12 min) due to the heat of fusion. Following this phenomenon, the deep foot temperatures continued to drop until bath temperature was reached (32 min). The foot remained at bath temperature for approximately 36 min.

Upon removal from the freezing bath and the protective rubber sleeve, the foot was frost covered, grey in color, and solid to the touch. The tourniquet was removed and rapid rewarming (in a 42°C water bath) was initiated immediately, requiring 18 to 21 min. There was a very slight plateau in the deep foot time-temperature curve between −5 and 0°C as the foot was being rewarmed. Immediately following this plateau, color began to return to the tissue, and evidence of edema was first noted. Thaw was considered complete when the injured foot reached the temperature of the contralateral foot. Maximum edema was reached by 30 to 60 min postthaw. Hyperemia was maximum at the time of removal from the warming bath and visible signs of tissue perfusion decreased from that point. Clear or serosan-

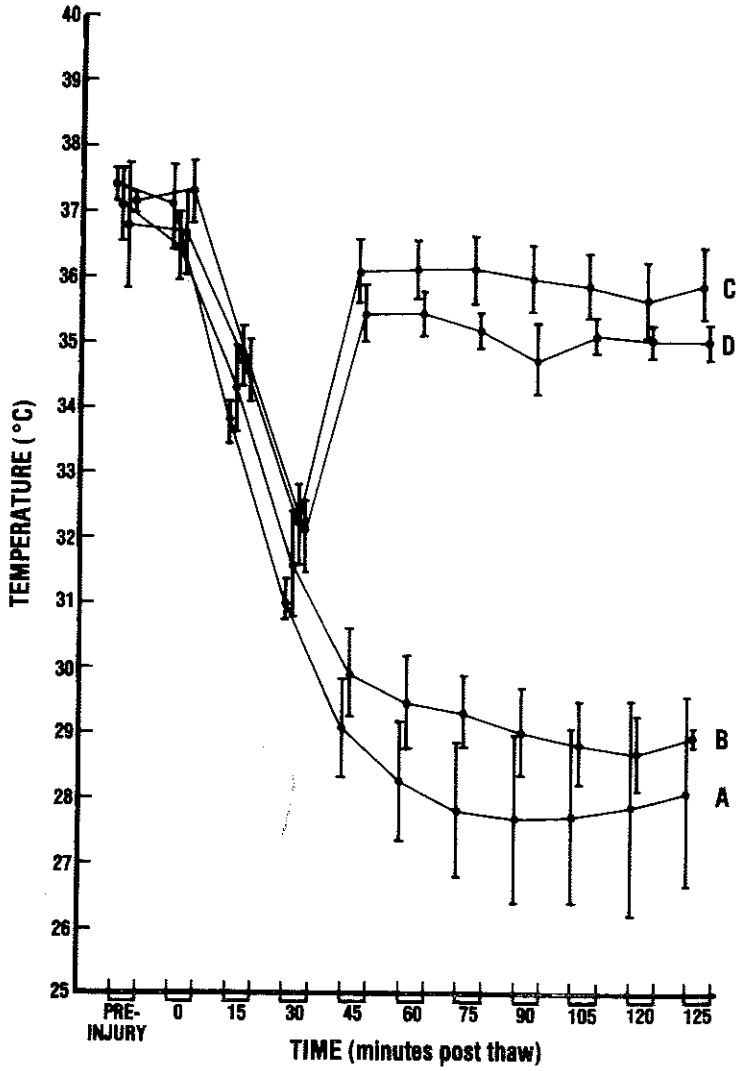

FIG. 4. Mean deep foot temperatures for control (A), vasodilator (B), fasciotomy (C), and fasciotomy-vasodilator (D) groups. Brackets indicate 1 SE.

guineous vesicles of 3 to 10 mm in diameter formed in the dorsal and plantar interdigital spaces within the first 2 hr postthaw. The vesicles ruptured or receded on Days 2 to 4 postthaw. Upon removal from the rewarming bath, left foot temperatures for all groups were between 36.7 and 37.3°C (Fig. 4). At 30 min postthaw, group means had fallen to between 31.1 and 32.2°C. By 45 min postthaw, the dogs receiving fasciotomy had injured foot temperatures of 36.1 (C) and 35.4 (D) while the nonfasciotomy dogs injured feet continued to cool to 29.1 (A) and 30.0 (B) ($P < 0.05$). By 2 hr post thaw, mean temperatures had stabilized at 35.7 (C) and 35.1 (D) for the dogs with fasciotomy, and 27.9 (A) 28.7 (B) ($P < 0.05$) for groups not receiving fasciotomy.

During the freezing period the tourniqueted contralateral (right) foot stabilized at ambient temperature. Upon removal of the tourniquet, the right foot experienced a transient hyperemia and re-

turn to preinjury temperature within 3 to 5 min. By 15 min postthaw, right foot temperatures dropped in all groups to 34.5 (A), 33.6 (B), 34.2 (C), and 34.4 (D). Right foot deep temperatures continued to drop sharply until 90 min postthaw when they stabilized at 29.3 (B), 27.5 (C), and 27.4 (D), while group A plateaued at 60 min at 32.6. The greatest reduction in group C and D right foot temperatures were observed immediately postfasciotomy when the left feet were increasing rapidly in temperature.

On Day 1 (18 to 24 hr postthaw) left foot temperatures for all groups were between 35.9 and 36.9°C (Fig. 5). Group A (control) temperatures dropped on Days 1 and 2 to stabilize between 32 to 33°C. Group B (vasodilator) temperatures remained at approximately 37°C through Day 2, then dropped to stabilize between 35 and 36°C. Group C (fasciotomy) maintained its temperature through Day 4, then dropped gradually to reach approximately 32°C on Day 12. Group D (fasciotomy/vasodilator) maintained its temperature

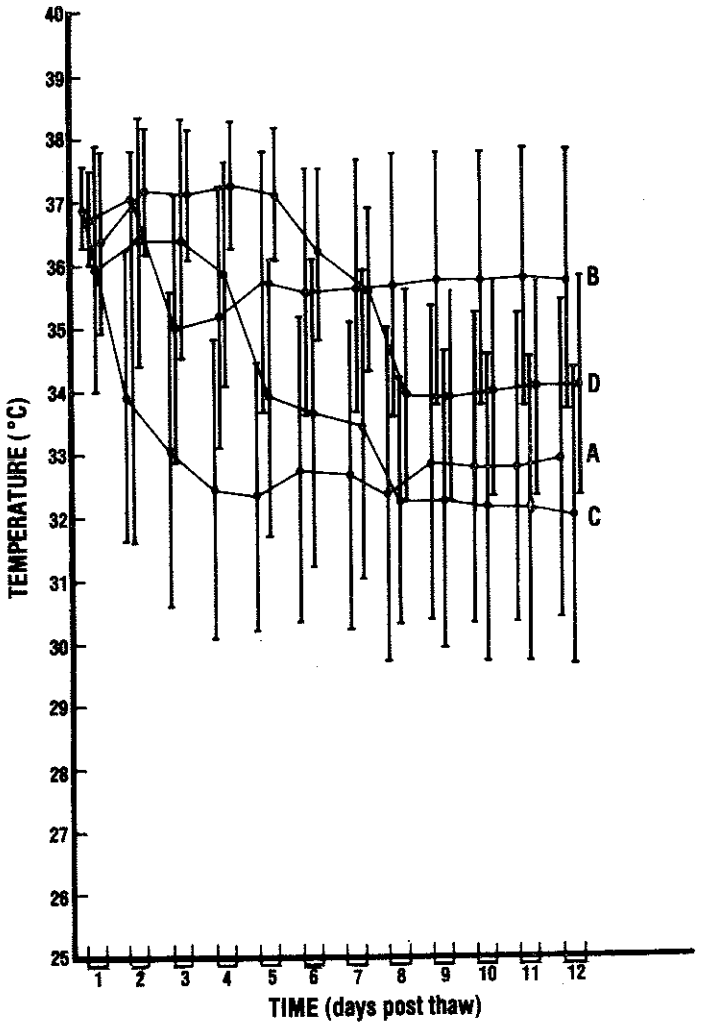

FIG. 5. Mean deep foot temperatures for control (A), vasodilator (B), fasciotomy (C), and fasciotomy/vasodilator (D) groups; Days 1 to 12. Brackets indicate 1 SE.

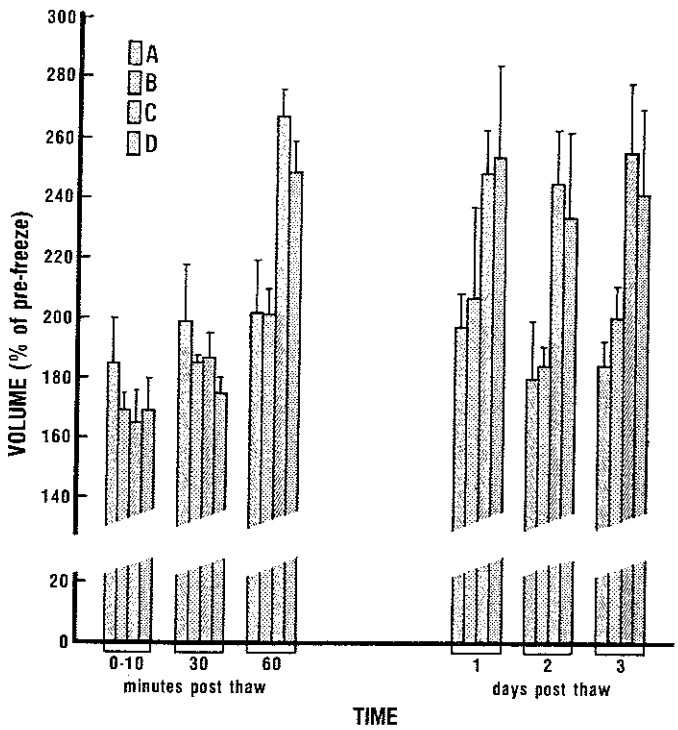

FIG. 6. Mean foot volumes (distal to tarsal-metatarsal junction) expressed as percent of preinjury values; control (A), vasodilator (B), fasciotomy (C), and fasciotomy/vasodilator (D). Brackets indicate 1 SE.

through Days 6 and 7 then dropped to stabilize at 34°C on Day 8.

Mean foot volumes, a measure of edema formation, reached 175 to 199% of their preinjury volumes by 30 postthaw (Fig. 6). One hour postthaw volumes of nonfasciotomy groups were 202% (A) and 201% (B) of preinjury while fasciotomy groups were 268% (C) and 249% (D) ($P < 0.05$). By Day 3 postthaw, foot volumes were 184% (A) and 200% (B); 256% (C) and 241% (D) ($P < 0.05$) of preinjury. Mean volumes beyond Day 3 are deceiving as large deviations within groups are evident.

Mean tissue pressures measured 59.0 (A), 44.8 (B), 63.0 (C), and 68.3 (D) cm of water at 25 min post thaw (Fig. 7). The 1 hr measurements were 63.8 (A), 54.0 (B), 18.0 (C), and 25.4 (D) cm of water. One hour measurements in groups C and D were taken 10 to 20 min after completion of fasciotomy and were significantly lower than nonfasciotomy groups ($P < 0.05$).

Surface bacterial infection was evident clinically within 2 to 3 days postthaw in all dogs. *Pseudomonas* sp. was the most common bacterial organism isolated. Severity of infection typically increased as judged by degree of pigment and plaque formation, to maximum on Days 5 to 7 and then gradually subsided. Dogs that went on to save large amounts of tissue, showed the greatest amount of pigment, for the longest period of time. Dogs whose feet mummified early showed evidence of infection only near the line of demarcation. In no case, however, was the degree of infection felt to be clinically significant.

Tissue survival at 14 days, scored for all animals, is listed in Fig. 8. Tissue survival was not significantly different between control and treatment groups.

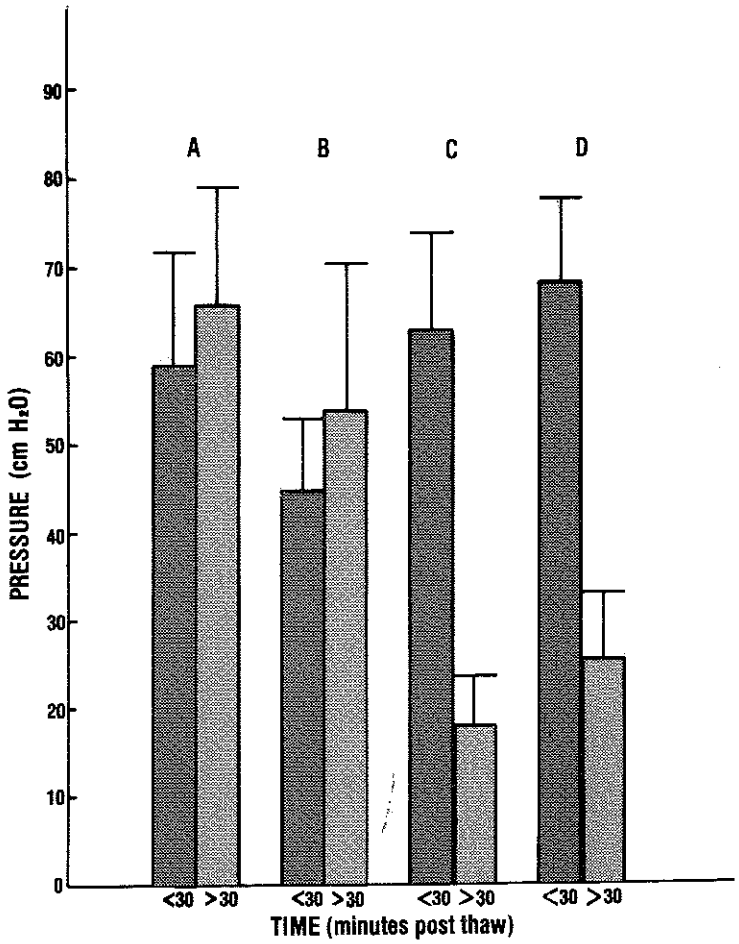

FIG. 7. Mean tissue pressures measured at 20 to 30 and 45 to 60 min postthaw for control (A), vasodilator (B), fasciotomy (C), and fasciotomy/vasodilator (D). Fasciotomy was completed between 30 and 45 min postthaw in groups C and D.

	Control (A)	Vasodilator (B)	Fasciotomy (C)	Fasciotomy/Vasodilator (D)
	5	6	8	9
	3	6	8	6
	3	5	3	5
	1	5	2	4
	1	3	1	2
	1	2	0	1
				1
				0
$\bar{X}$	2.33	4.50	3.67	3.50
S_x	1.63	1.64	3.50	3.07
$S_{\bar{x}}$	0.67	0.67	1.43	1.09

FIG. 8. Fourteen day tissue loss/survival score based on grading key (Fig. 2). Though highest mean scores were found in vasodilator group (B), it should be noted that best individual dogs were found in groups C and D.

DISCUSSION

The goals of this study were: (1) to develop a chronic dog model for frostbite investigation, and (2) to evaluate fasciotomy as a treatment for frostbite utilizing that model. Since vasodilator therapy currently is used clinically in the treatment of frostbite, it was deemed necessary to evaluate fasciotomy as an adjunct to this already existing therapeutic modality. Thus, four groups were studied: control treatment (A), vasodilator only (B), fasciotomy only (C), and fasciotomy and vasodilator (D). In developing a chronic dog model for frostbite, the freezing bath temperature and time described by Sumner (12) was utilized initially. Sumner's 70 min injury produced only a superficial injury in our dogs. This may be explained by the fact that nursing care was minimal in the previous study, i.e., no whirlpool or bandaging. In the Sumner study, a still bath was used, while our bath was circulated to break up thermal layering. Recent work has shown significantly reduced warming rates using uncirculated rewarming bath with no foot movement vs whirlpool or even rotation of the foot in a still bath (5). Consequently, to produce the same injury as the previous study (12), a much more severe time-temperature relationship was required. We attribute this difference to the nursing care provided and cannot overemphasize the apparent clinical importance of nursing care in the management of frostbite.

After immersion in the rewarming bath, the frozen feet remained gray and stiff until warmed above 0°C. Very shortly after passing the plateau representing conversion of ice to water (approx., 12 min into thaw), the foot became hyperemic and pliable. By the time the frozen foot reached the temperature of the contralateral foot, it showed marked edema and by 60 min postthaw it reached maximum edema. Subsequent electromagnetic flow measurements have indicated that return of blood flow to the injured limb immediately follows the plateau in temperature during thaw (5). Flow return in severely injured limbs equalled or exceeded prefreeze flow for 15 to 30 min then dropped markedly. Rabb (11) has described similar fluctuations in flow at the microcirculatory level. We believe the early visible hyperemia, edema formation, and subsequent cyanosis results from a rather orderly pathologic scheme: return of flow beyond prefreeze rates following rewarming, venular and venous sludging, pressure changes, endothelial permeability changes, extravasation of fluids from capillaries and arterioles, and eventual venular and venous then capillary and arteriolar stasis.

Contralateral foot temperatures suggest that blood flow to one hind limb influences flow to the other. This is best illustrated by the increased rate of cooling of group C and D right feet following fasciotomy. Because of prefasciotomy increased tissue pressures in the left leg, a greater blood volume, as indicated by foot temperature, entered the right leg than the left. As left leg tissue pressures were reduced by fasciotomy in group C and D dogs, blood flow was reduced in the right limb. A possible explanation for this apparent flow rate reversal is a centrally mediated reflex in response to fasciotomy-induced volume loss, superimposed on local postischemic hyperemia. Group A, maintaining the increased tissue pressure of the left limb, as expected maintained the highest right foot temperature. The fact that group B (vasodilator only) right and left foot temperatures remained very nearly the same through the first 90 min may result from the α-adrenergic blockade overriding the effect of increased tissue pressure to some degree.

One may question why such a severe injury was produced in this study. Three factors influenced this decision. First, severe injuries can be reproduced consistently in the laboratory. Conditions that produce moderate injury often result in variable degrees of tissue loss. Second, it was felt that if fasciotomy was found to be

useful clinically in severe frostbite, its utility could be extended to lesser injuries in which the degree of tissue compression is still significant. Third, severe frostbite itself is a serious clinical problem.

The dog was selected as the animal model because of its size, availability, and anatomical and physiological similarities to man. One shortcoming of the dog is a dissimilarity in vascular tone compared to man. For this reason, a tourniquet was applied during the freezing period to compensate the dog's failure to vasoconstrict peripherally during cold exposure.

A major advantage of a dog model is the contracted time course of frostbite pathophysiology compared to that observed in man. The following times may be considered comparable: maximum edema 0.5 to 1 hr (dog), 36 to 48 hr (man); vesicle rupture 2 to 4 days (dog), 4 to 10 days (man); eschar separation 10 to 14 days (dog), 20 to 30 days (man). These times explain why fasciotomy was performed one half hour after thawing.

During the course of this study, changes in foot volume became our most accurate prognostic indicator of the status of the local circulatory system in individual dogs. Twenty-four to 48 hr before marked drop in foot temperature and tissue death, a marked reduction in foot volume was seen. This may be explained by a simple reduction in local blood flow, thus in pressure gradient across damaged capillary membranes. Fasciotomy dogs which salvaged their entire feet showed the greatest swelling from Day 1, sometimes to the point that a second fasciotomy seemed indicated. Several of the dogs from group C and D who eventually lost the entire foot showed complete lack of edema, distal to the future auto-amputation line on Day 1 following thaw.

Vesicle formation was not readily comparable to that seen in human frostbite. In the dog, vesicles are approximately 4 to 6 mm in diameter, of split thickness, containing serosanguineous fluid. Vesicles were found only in the interdigital spaces on plantar or dorsal surfaces on the dog foot, while in man they are normally seen over the dorsal finger tip first, progressing proximally with increased injury, and not seen at all in very severe injury. This difference in vesicles may be due to species variation in the skin anatomy (i.e., increased collagen/elastic fiber ratio in the dog) and pattern of blood supply. There was no apparent correlation between the final outcome and either size of vesicles or appearance of their fluid contents.

The second goal of this study was the evaluation of three modes of therapy for frostbite: vasodilator (B), fasciotomy (C), and fasciotomy/vasodilator combined (D). Early indicators of increased blood supply following fasciotomy were encouraging: deep foot temperatures increased significantly. This improvement was reflected clinically by pink color, decreased capillary refill time, palpable arterial pulse, and edema. The marked reduction in post-fasciotomy tissue pressures in groups C and D was accompanied by increased foot temperatures, consistent with the hypothesis that fasciotomy reduced physical compression on blood vessels. Increased foot temperatures due to fasciotomy were maintained for 2 to 5 days following frostbite injury. This temperature data strongly suggests that the integrity of the circulation to the foot was prolonged. It cannot be ruled out that the early improvement resulted from arterial-venous shunting post-fasciotomy, and that warmed tissue is not necessarily perfused tissue. This is probably true in part, since the overall tissue survival was not significantly improved as a result of fasciotomy.

In spite of the less than remarkable overall tissue outcome, these data none-the-less support the thesis that fasciotomy may have a role in frostbite therapy. A pattern of tissue loss was apparent in the dog frostbite model: fasciotomy was either markedly successful or appeared to be counterproductive for tissue salvage. The

very favorable results in several of the fasciotomy dogs is important because the injury produced in all animals was exteremely severe, and resulted in autoamputation at the tarsal-metatarsal junction in control animals. Only the few dogs in groups C and D survived with an essentially intact foot after injury. Why the fasciotomy appeared to be an all or nothing therapy is not clear. The feet which mummified early appear either to have failed to reestablish nutritive flow, or to have sustained direct effects of freezing of cells, or both. The feet which remained viable for 2 to 5 days postfreeze, then deteriorated seem to have survived the direct effect of freezing, but succumbed to some later circulatory pathology. Further studies are necessary to increase our understanding of the pathophysiology leading to the breakdown of an apparently improved postfasciotomy vascular system in the frostbitten limb.

SUMMARY

Severe freezing injury was produced in the hind foot of 26 mongrel dogs. All dogs were given daily whirlpool treatment and protective bandaging for 14 days following injury. In addition, certain dogs received a vasodilator, fasciotomy, or both vasodilator and fasciotomy following injury. Deep foot temperatures, foot volumes, tissue pressures, and 14 day tissue loss-salvage scores were compared. Significant differences between fasciotomy and nonfasciotomy dogs were seen in foot temperature, volume, and tissue pressure immediately following fasciotomy. Though there was no significant difference in 14 day tissue loss, there was clinically apparent prolongation of integrity of the local vascular system for 2 to 5 days following fasciotomy, and total foot salvage in several dogs receiving fasciotomy.

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